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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/689,530	10/17/2003	Timothy J. Cardozo	05986/100M127-US1	8661

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EXAMINER	
KHARE, DEVESH	

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 05/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/689,530	CARDOZO ET AL.	
	Examiner	Art Unit	
	Devesh Khare	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-29 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-29 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 4/7/2004.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Claims 1-29 are before the examiner and an action on the merits of said claims is contained herein below.

Minor objections

Claims 2 and 9 are objected to because of the following informalities:

(1) In claim 2, the abbreviations "TS-1" and "FdUMP" should be preceded in their first occurrence by the specific identity of the entities said abbreviations are intended to represent in the claims. Thereafter, the use of the abbreviation in the claims will be favorably considered and explicitly understood.

(2) In claims 2 and 9, line 3, the term "-" is missing before FU.

Appropriate correction is required.

35 U.S.C. 112, second paragraph rejection

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims **1-29** are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(A) Claims 1,8, 27 and 28 are rejected, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: pharmaceutical carrier. Claims 1,8, 27 and 28 should contain more than one component, and the additional component should be

enabled. In other words, the critical element, which is an acceptable pharmaceutical carrier for the specific active agent should be set forth.

(B) Claims 8,27 and 28 are vague and indefinite as it is unclear to whom the 5-fluorouracil prodrug is being administered.

Claims which depend from an indefinite claim which fail to obviate the indefiniteness of the claim from which they depend are also seen to be indefinite and are also rejected for the reasons set forth supra.

35 U.S.C. 103(a) rejection

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hostetler (U.S.Patent 5,654,286) in view of Spector et al. (Spector) (U.S. Patent 6,297,223) in combinations with Bissery (U.S. Patent 6,664,242).

Claims 1-29 are drawn to methods for treating an inflammatory skin condition in a patient (claim 1) and treating psoriasis (claim 8) which comprises orally administering an effective amount of a prodrug of 5-fluorouracil or a transdermal prodrug of 5-fluorouracil (claim 27) or a transmucosal prodrug of 5-fluorouracil (claim 28). Dependent claim limitations include the oral prodrug of 5-fluorouracil is selected from the group consisting

of capecitabine, 5-fluoro-pyrimidinone, TS-1, FdUMP, 1-(2'-oxopropyl)-5-FU, and alkyl-carbonyl-5-FU (claims 2 and 9); the inflammatory skin condition is selected from the group of claim 3; the effective amount in a non-pulse dosing regimen is between 5 and 2500 mg per square meter of body surface area per day (claims 4-7,10-13 and 16-18); the effective amount of pulse dosing regimen is between 5 and 5000 mg per square meter of body surface area per day (claims 19-22) and the effective amount of capecitabine in non-pulse dosing regimen is between 5 and 2500 mg per square meter of body surface area per day (claims 14-18) and in pulse dosing regimen is between 100 and 5000 mg per square meter of body surface area per day (claims 23-26).

Hostetler teaches the topical treatment of the diseases of skin cell hyperproliferation such as psoriasis using pharmaceutical compositions containing nucleoside analog phosphate ester and related analogs (abstract). Hostetler discloses that the topical use of 5-flurouracil has not been very successful in the treatment to reduce skin inflammation (col. 1, lines 55-65). The topical use of an anti-psoriasis agent such as 5-flurouracil phosphate ester is disclosed (cols. 5-6, lines 65 thru lines 1-10). Hostetler disclose the dosage between 0.1 gm % and 10 gm % for application to an area of skin (col.3, lines 5-15). Hostetler differs from the applicant's invention in that Hostetler does not disclose a prodrug of 5-fluorouracil and its oral use in the treatment of psoriasis.

Spector teaches the oral administration of a prodrug of 5-fluorouracil in the treatment of psoriasis or rheumatoid arthritis (col. 1, lines 50-55). The prodrugs of uracil derivatives are disclosed (col. 2, line 40). The prodrug of 5-fluorouracil may be

administered by oral, rectal, nasal, topical, vaginal, and parenteral modes (col. 2, lines 55-60). The dosage is disclosed in the range of 0.1 to 3000 mg per kilogram body weight (col.3, lines 15-20). Spector does not disclose specifically the use of capecitabine.

Bissery teaches the use of capecitabine for its anti-neoplastic activity (cols. 3-4, lines 65 and 1-15). Bissery discloses that capecitabine has more favourable safety profile than 5- flurouracil (col.3, lines 25-30).

Therefore, one of ordinary skill in the art would have found the applicant's methods for treating an inflammatory skin condition in a patient and treating psoriasis which comprises orally administering an effective amount of a prodrug of 5-fluorouracil or a transdermal prodrug of 5-fluorouracil or a transmucosal prodrug of 5-fluorouracil, to have been obvious at the time the invention was made having the above cited references before him. Since Hostetler discloses that the topical use of 5-flurouracil has not been very successful in the treatment to reduce skin inflammation; Spector teaches the oral administration of a prodrug of 5-fluorouracil in the treatment of psoriasis or rheumatoid arthritis and Bissery discloses that capecitabine has more favourable safety profile than 5- flurouracil, one skilled in the art would have a reasonable expectation for success in combining the teachings of these references to accomplish a method for treating an inflammatory skin condition such as psoriasis in a patient which comprises orally administering an effective amount of a prodrug of 5-fluorouracil. The motivation

for doing so is provided by Hostetler and Spector references, Hostetler discloses that the topical use of 5-flurouracil has not been very successful in the treatment to reduce skin inflammation (col. 1, lines 55-65) and Spector discloses the oral use of a prodrug of 5-fluorouracil in the treatment of psoriasis or rheumatoid arthritis (col. 1, lines 50-55).

Any inquiry concerning this communication or earlier communications from the

Examiner should be directed to Devesh Khare whose telephone number is 571-272-0653. The examiner can normally be reached on Monday to Friday from 8:00 to 4:30. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson, Supervisory Patent Examiner, Art Unit 1623 can be reached at 571-272-0661. The official fax phone numbers for the organization where this application or proceeding is assigned is (703) 308-4556 or 308-4242.
Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Devesh Khare, Ph.D.,J.D.
Art Unit 1623
April 26,2005

JAMES O. WILSON
SUPERVISORY PATENT EXAMINER
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